

WHAT IS CLAIMED:

1. A recombinant adeno-associated viral vector comprising at least a first nucleic acid
5 segment encoding a biologically-active Factor VII peptide, polypeptide or protein
operably linked to at least a first promoter capable of expressing said segment in a
mammalian host cell transformed with said vector.
- 10 2. The recombinant adeno-associated viral vector of claim 1, wherein said nucleic acid
segment encodes a mammalian biologically-active Factor VII peptide, polypeptide or
protein.
- 15 3. The recombinant adeno-associated viral vector of claim 2, wherein said nucleic acid
segment encodes a biologically-active Factor VII peptide, polypeptide or protein that
comprises a first contiguous sequence region of at least 60 amino acids from any one
of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ
ID NO:12, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:15 or SEQ ID NO:17.
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4. The recombinant adeno-associated viral vector of claim 3, wherein said nucleic acid
segment encodes a biologically-active Factor VII peptide, polypeptide or protein that
comprises at least a first contiguous sequence region of at least 80 amino acids from
25 any one of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID

NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:15 or SEQ ID NO:17.

- 5 5. The recombinant adeno-associated viral vector of claim 4, wherein said nucleic acid segment encodes a biologically-active Factor VII peptide, polypeptide or protein that comprises at least a first contiguous sequence region of at least 100 amino acids from any one of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:15 or SEQ ID
- 10 NO:17.
6. The recombinant adeno-associated viral vector of claim 5, wherein said nucleic acid segment encodes a biologically-active Factor VII peptide, polypeptide or protein that
- 15 comprises at least a first contiguous sequence region of at least 120 amino acids from any one of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:15 or SEQ ID
- NO:17.
- 20 7. The recombinant adeno-associated viral vector of claim 6, wherein said nucleic acid segment encodes a biologically-active Factor VII peptide, polypeptide or protein that comprises the sequence of any one of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15,
- 25 SEQ ID NO:15 or SEQ ID NO:17.

8. The recombinant adeno-associated viral vector of claim 6, wherein said nucleic acid segment encodes a biologically-active Factor VII peptide, polypeptide or protein that comprises the sequence of any one of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:15 or SEQ ID NO:17.

9. The recombinant adeno-associated viral vector of claim 1, wherein said nucleic acid segment encodes a biologically-active human Factor VII peptide, polypeptide or protein.

10. The recombinant adeno-associated viral vector of claim 9, wherein said nucleic acid segment encodes a biologically-active human Factor VII peptide, polypeptide or protein that comprises the sequence of SEQ ID NO:2.

11. The recombinant adeno-associated viral vector of claim 3, wherein said nucleic acid segment comprises at least a first contiguous sequence region of at least 180 nucleotides from any one of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13.

12. The recombinant adeno-associated viral vector of claim 11, wherein said nucleic acid segment comprises at least a first contiguous sequence region of at least 210 nucleotides from any one of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13.

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13. The recombinant adeno-associated viral vector of claim 12, wherein said nucleic acid segment comprises at least a first contiguous sequence region of at least 240 nucleotides from any one of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13.

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14. The recombinant adeno-associated viral vector of claim 13, wherein said nucleic acid segment comprises at least a first contiguous sequence region of at least 270 nucleotides from any one of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13.

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15. The recombinant adeno-associated viral vector of claim 14, wherein said nucleic acid segment comprises at least a first contiguous sequence region of at least 300 nucleotides from any one of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13.

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16. The recombinant adeno-associated viral vector of claim 15, wherein said nucleic acid segment comprises the nucleotide sequence of any one of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13.

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17. The recombinant adeno-associated viral vector of claim 16, wherein said nucleic acid segment comprises the nucleotide sequence of SEQ ID NO:1.

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18. The recombinant adeno-associated viral vector of claim 1, wherein said promoter is a heterologous promoter.

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19. The recombinant adeno-associated viral vector of claim 18, wherein said promoter is selected from the group consisting of a CMV promoter, a β -actin promoter, a hybrid CMV promoter, a hybrid β -actin promoter, an EF1 promoter, a U1a promoter, a U1b promoter, a Tet-inducible promoter and a VP16-LexA promoter.

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20. The recombinant adeno-associated viral vector of claim 19, wherein said promoter is a chicken β -actin promoter.

21. The recombinant adeno-associated viral vector of claim 1, wherein said vector further comprises at least a first enhancer.
- 5 22. The recombinant adeno-associated viral vector of claim 21, wherein said vector further comprises a CMV enhancer, a synthetic enhancer, a muscle-specific enhancer, a liver-specific enhancer, or a tissue-specific enhancer.
- 10 23. The recombinant adeno-associated viral vector of claim 1, wherein said vector further comprises at least a first intron sequence.
- 15 24. The recombinant adeno-associated viral vector of claim 1, wherein said polynucleotide further comprises a 3' regulatory element operably linked to said nucleic acid segment.
- 20 25. The recombinant adeno-associated viral vector of claim 24, wherein said 3' regulatory element comprises a woodchuck hepatitis virus post-transcriptional regulatory element (WPRE).
- 25 26. The recombinant adeno-associated viral vector of claim 1, wherein said nucleic acid segment is obtained from a human, primate, murine, porcine, bovine, ovine, canine, feline, equine, epine, caprine, avian, or lupine source.

27. The recombinant adeno-associated viral vector of claim 1, wherein said nucleic acid segment encodes a biologically-active mammalian Factor VII polypeptide that is at least 85% identical to the amino acid sequence of any of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:15 or SEQ ID NO:17.

28. The recombinant adeno-associated viral vector of claim 27, wherein said nucleic acid segment encodes a biologically-active mammalian Factor VII polypeptide that is at least 90% identical to the amino acid sequence of any of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:15 or SEQ ID NO:17.

29. The recombinant adeno-associated viral vector of claim 28, wherein said nucleic acid segment encodes a biologically-active mammalian Factor VII polypeptide that is at least 95% identical to the amino acid sequence of any of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:15 or SEQ ID NO:17.

30. The recombinant adeno-associated viral vector of claim 29, wherein said nucleic acid segment encodes a biologically-active mammalian Factor VII polypeptide that is at least 98% identical to the amino acid sequence of any of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:15 or SEQ ID NO:17.

31. The recombinant adeno-associated viral vector of claim 1, wherein said nucleic acid segment encodes a biologically-active mammalian Factor VII polypeptide that is at least 85% identical to the amino acid sequence of SEQ ID NO:2.

32. The recombinant adeno-associated viral vector of claim 31, wherein said nucleic acid segment encodes a biologically-active mammalian Factor VII polypeptide that is at least 88% identical to the amino acid sequence of SEQ ID NO:2.

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33. The recombinant adeno-associated viral vector of claim 32, wherein said nucleic acid segment encodes a biologically-active mammalian Factor VII polypeptide that is at least 91% identical to the amino acid sequence of SEQ ID NO:2.

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34. The recombinant adeno-associated viral vector of claim 33, wherein said nucleic acid segment encodes a biologically-active mammalian Factor VII polypeptide that is at least 94% identical to the amino acid sequence of SEQ ID NO:2.

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35. The recombinant adeno-associated viral vector of claim 34, wherein said nucleic acid segment encodes a biologically-active mammalian Factor VII polypeptide that is at least 97% identical to the amino acid sequence of SEQ ID NO:2.

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36. The recombinant adeno-associated viral vector of claim 1, comprised within an adeno-associated viral particle.

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37. The recombinant adeno-associated viral vector of claim 36, wherein said viral particle is an adeno-associated viral serotype 1 (AAV1), serotype 2 (AAV2), serotype 3 (AAV3), serotype 4 (AAV4), serotype 5 (AAV5), or serotype 6 (AAV6) viral particle.

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38. The recombinant adeno-associated viral vector of claim 1, comprised within an isolated mammalian host cell.

5 39. A recombinant adeno-associated virion comprising the recombinant adeno-associated viral vector of claim 1.

10 40. A plurality of recombinant adeno-associated viral particles comprising the recombinant adeno-associated viral vector of claim 1.

15 41. A host cell comprising: (a) the recombinant adeno-associated viral vector of claim 1; (b) the virion of claim 39; or (c) the plurality of viral particles of claim 40.

20 42. The host cell of claim 41, wherein said host cell is a bone marrow, liver, kidney, spleen, endothelial, epithelial, heart, lung, pancreatic, cancer, tumor, bone, or blood cell.

43. The host cell of claim 42, wherein said host cell is a human cell.

25 44. The host cell of claim 43, wherein said host cell is a human liver cell.

45. A composition comprising: (a) the recombinant adeno-associated viral vector of claim 1; (b) the virion of claim 39; (c) the plurality of viral particles of claim 40, or the host cell of claim 41.

46. The composition of claim 45, further comprising a pharmaceutical excipient.

47. The composition of claim 45, further comprising a microparticle, nanoparticle, microsphere, nanosphere, liposome, lipid, or lipid complex.

48. The composition of claim 45, for use in therapy.

49. The composition of claim 48, for use in the therapy of hemophilia or Factor VII deficiency.

50. The composition of claim 49, for use in the therapy of human hemophilia or human Factor VII deficiency.

51. A kit for treating or ameliorating the symptoms of Factor VII deficiency in a mammal comprising (1) the recombinant adeno-associated viral vector of claim 1; the virion of

claim 39; the plurality of viral particles of claim 40; the host cell of claim 41; or the composition of claim 45; and (2) instructions for using said kit.

5 52. Use of the recombinant adeno-associated viral vector of claim 1, the virion of claim 39, the plurality of viral particles of claim 40, the host cell of claim 41, or the composition of claim 45, in the manufacture of a medicament for treating hemophilia, Factor VII deficiency, or a bleeding disorder in a mammal.

10 53. The use according to claim 52, wherein said vector, said virion, said particle, said host cell, or said composition is provided to said mammal by injection, infection, or direct administration to a cell, tissue, or organ of said mammal.

15 54. The use according to claim 53, wherein said mammal is human.

20 55. The use according to claim 54, wherein said mammal is a human that has, is suspected of having, or at risk for developing hemophilia A.

25 56. A method for providing an animal a biologically-active Factor VII peptide or polypeptide, said method comprising administering to said mammal: (a) the recombinant adeno-associated viral vector of claim 1; (b) the virion of claim 39; (c) the plurality of viral particles of claim 40; (c) the host cell of claim 41; or (d) the composition of claim 45, in an amount and for a time sufficient to provide said mammal with an effective amount of said biologically-active Factor VII peptide or polypeptide.

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57. The method of claim 56, wherein said mammal has, is at risk for developing, or is diagnosed with hemophilia.

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58. A method for treating or ameliorating the symptoms of a Factor VII polypeptide defect, deficiency or dysfunction in a mammal, said method comprising administering to said mammal: (a) the recombinant adeno-associated viral vector of claim 1; (b) the virion of claim 39; (c) the plurality of viral particles of claim 40; (c) the host cell of claim 41; or (d) the composition of claim 45, in an amount and for a time sufficient to treat or ameliorate the symptoms of said defect, deficiency or dysfunction in said mammal.

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15 59. The method of claim 58, wherein said mammal has, is at risk for developing, or is diagnosed with hemophilia, a clotting deficiency, or a bleeding disorder.

60. A method for treating or ameliorating the symptoms of hemophilia in a mammal, said method comprising administering to said mammal: (a) the recombinant adeno-associated viral vector of claim 1; (b) the virion of claim 39; (c) the plurality of viral particles of claim 40; (c) the host cell of claim 41; or (d) the composition of claim 45, in an amount and for a time sufficient to treat or ameliorate the symptoms of hemophilia in said mammal.

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61. The method of claim 60, wherein said mammal has, is at risk for developing, or is diagnosed with hemophilia A.

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62. The method of claim 60, wherein said composition is administered to said human intramuscularly, intravenously, or by injection to at least one cell, tissue, or organ of said human.

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63. The method of claim 60, wherein said vector, said virion, said particle, said cell, or said composition is provided to said mammal systemically, or by direct or indirect administration to a cell, tissue, or organ of said mammal.

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64. The method of claim 63, wherein said vector, said virion, said particle, said cell, or said composition is provided to mammal by direct injection into the muscle tissue, or the liver of said mammal.